Claims

WE CLAIM:

1. Isolated nucleic acid encoding a murine IRAK-M protein comprising the nucleic acid sequence depicted in SEQ ID NO.: 1.

2. Isolated nucleic acid that encodes a murine IRAK-M protein comprising the amino acid sequence depicted in SEQ ID NO.: 2.

3. Isolated IRAK-M protein encoded by the nucleic acid sequence depicted in SEQ ID NO.: 1.

4. Isolated IRAK-M protein comprising the amino acid sequence depicted in SEQ ID NO.: 2.

5. An expression vector comprising the nucleic acid which has the sequence depicted in SEQ ID NO.: 1.

6. An expression vector comprising nucleic acid encoding the amino acid sequence depicted in SEQ ID NO.: 2.

7. The vector of claim 5 further comprising DNA sufficient for expression of the DNA encoding the amino acid sequence depicted in SEQ ID NO.: 2.

8. A cell transformed with the vector of claim 5.

9. A cell transformed with the vector of claim 6.

10. A cell transformed with the vector of claim 7.

11. A method for producing murine IRAK-M comprising culturing cells that contain a vector comprising DNA encoding murine IRAK-M under

conditions appropriate for expression of the DNA, wherein murine IRAK-M is thereby produced.

12. An isolated cell which does not comprise nucleic acid encoding a functional IRAK-M.

13. An isolated IRAK-$M^{-/-}$ cell.

14. A method of identifying a compound that modulates the innate immune response in an individual, comprising combining cells expressing murine IRAK-M with a candidate compound, and determining whether the candidate compound modulates IRAK-M activity in the cells, wherein modulation of IRAK-M activity in the cells by the candidate compound indicates that the candidate compound modulates the innate immune response in the individual.

15. A method of identifying a compound that produces an anti-inflammatory effect and an immunoinhibitory effect in a subject, comprising combining cells expressing IRAK-M with a candidate compound and determining whether the candidate compound enhances IRAK-M activity in the cells, wherein if enhancement of IRAK-M activity occurs in the cells, a candidate compound that produces an anti-inflammatory effect and an immunoinhibitory effect is identified.

16. A method of identifying a compound that produces an immunostimulatory effect in a subject, comprising combining cells expressing IRAK-M with a candidate compound and determining whether the candidate compound inhibits IRAK-M activity in the cells, wherein if inhibition of IRAK-M activity occurs in the cells, a compound that produces an immunostimulatory effect is identified.

17. A method of producing an anti-inflammatory effect and an immunoinhibitory effect in an individual, comprising administering to the

individual a compound that enhances IRAK-M in cells in sufficient quantity to enhance IRAK-M, thereby producing an anti-inflammatory effect and an immunoinhibitory effect in the individual.

18. A method of treating an inflammatory condition in an individual comprising administering to the individual a compound that enhances IRAK-M activity in the cells in the individual thereby producing an anti-inflammatory effect in the individual.

19. A method of determining whether a compound is an IRAK-M inhibitor, comprising:

(a) contacting a cell expressing IRAK-M with a candidate compound and measuring the production by the cell of an inflammatory cytokine or chemokine upon stimulation with a TLR or IL-1R ligand;

(b) comparing production by the cell of the inflammatory cytokine or chemokine in (a) with production by the cell of the inflammatory cytokine or chemokine in the absence of the candidate compound;

(c) contacting a cell which does not express IRAK-M with the candidate compound and measuring production by the cell of an inflammatory cytokine or chemokine upon stimulation with a TLR or IL-1R ligand; and

(d) comparing production by the cell of the inflammatory cytokine or chemokine in (c) with production by the cell of the inflammatory cytokine or chemokine in the absence of the candidate compound,

wherein if production in (a) which is more than production in (b), and the production in (c) which is comparable to production in (d) indicates that the compound is an IRAK-M inhibitor.

20. A method of determining whether a compound is an IRAK-M inhibitor comprising:

(a) contacting a cell expressing IRAK-M with the candidate compound and measuring production by the cell of an inflammatory cytokine or chemokine upon stimulation with a pathogen;

(b) comparing production by the cell of the inflammatory cytokine or chemokine of step (a) with production by the cell of the inflammatory cytokine or chemokine in the absence of the candidate compound;

(c) contacting a cell which does not express IRAK-M with the candidate compound on a measuring production by the cell of an inflammatory cytokine or chemokine upon stimulation with a pathogen;

(d) comparing production by the cell of the inflammatory cytokine or chemokine in step (c) with production by the cell of the inflammatory cytokine or chemokine in the absence of the candidate compound.

wherein if production in (a) which is more than production in (b), and production in (c) which is comparable to the production in (d) indicates that the compound is an IRAK-M inhibitor.

21. A method of determining whether a compound is an IRAK-M inhibitor comprising:

(a) contacting a cell expressing IRAK-M with the candidate compound and measuring NF-κB activation in the cell;

(b) comparing the NF-κB activation measured in (a) with the activation of NF-κB measured in a cell expressing IRAK-M in the absence of the candidate compound;

(c) contacting a cell which does not express IRAK-M with the candidate compound and measuring the activation of NF-κB in the cell;

(d) comparing the NF-κ B activation measured in (c) with the NF-κ B activation measured in a cell which does not express IRAK-M in the absence of the candidate compound;

wherein the activation measured in (a) which is more than the activation measured in (b), and the activation measured in (c) which is comparable to the activation measured in (d) indicates that the compound is an IRAK-M inhibitor.

22. A method of detecting an agonist of IRAK-M activity, comprising:

(a) contacting a cell expressing IRAK-M with a candidate compound and measuring production of an inflammatory cytokine or chemokine upon stimulation with a TLR or IL-1R ligand; and

(b) comparing production by the cell of an inflammatory cytokine or chemokine in (a) with the production by the cell of the inflammatory cytokine or chemokine in the absence of the candidate compound,

wherein if production in (a) which is less than production in (b) indicates that the compound is an IRAK-M agonist.

23. A method of detecting an agonist of IRAK-M activity, comprising:

(a) contacting a cell expressing IRAK-M with a candidate compound and measuring production of an inflammatory cytokine or chemokine upon stimulation with a pathogen; and

(b) comparing production by the cell of an inflammatory cytokine or chemokine in (a) with the production by the cell of the inflammatory cytokine or chemokine in the absence of the candidate compound,

wherein if production in (a) which is less than production in (b) indicates that the compound is an IRAK-M agonist.

24. A method of determining whether a compound is an IRAK-M agonist comprising:

(a) contacting a cell expressing IRAK-M with the candidate compound and measuring NF-κB activation in the cell; and

(b) comparing the NF-κB activation measured in (a) with the activation of NF-κB measured in a cell expressing IRAK-M in the absence of the candidate compound;

wherein the activation measured in (a) which is less than the activation measured in (b), indicates that the compound is an IRAK-M agonist.